COMMENTARY

Advancing Dengue Prevention: Vaccine Development and Current Trials

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CITATION
Sharma N, Singh M, Aggarwal P. Advancing Dengue Prevention: Vaccine Development and Current Trials. Journal of the Epidemiology Foundation of India. 2025;3(2):200-202.
DOI: https://doi.org/10.56450/JEFI.2025.v3i02.015

ARTICLE CYCLE
Received: 15/06/2025; Accepted: 21/06/2025; Published: 30/06/2025

Abstract
Dengue fever remains one of the most significant mosquito-borne viral diseases, affecting nearly 390 million individuals annually, with 96 million symptomatic cases. In the absence of targeted antiviral therapy and the limitations of existing vector control strategies, vaccine development has emerged as the primary strategy for long-term dengue prevention. This manuscript reviews the global necessity for a dengue vaccine, discusses challenges related to immunological responses and antibody-dependent enhancement (ADE), and evaluates current vaccine candidates and ongoing clinical trials. Recent progress with licensed vaccines, such as Dengvaxia and Qdenga, is analyzed, along with promising developments from the NIH and Butantan Institute. Emerging platforms, including mRNA-based vaccines, have also been addressed.

Keywords
Dengue, Vaccine; Clinical Trials; Dengvaxia; Qdenga; Mrna; Tetravalent Vaccine; Antibody-Dependent Enhancement

Introduction
Dengue is a mosquito-borne viral illness primarily spread by Aedes aegypti mosquitoes and is prevalent in over 100 countries. Acute fever to more severe diseases, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), are among its effects. The World Health Organization (WHO) emphasizes how crucial it is to create a safe and efficient dengue vaccine to lessen the disease's increasing negative effects on health and the economy. (1,2).

The Imperative for a Dengue Vaccine
Symptomatic care and vector control are the mainstays of current dengue management. However, a preventive strategy by vaccination is required due to high cost, limited effectiveness of vector control initiatives, and mosquito's increased geographic range because of climate change (3) The four different serotypes of the virus (DENV-1 to DENV-4) present a significant immunological challenge since illness severity can be increased by immunity to one serotype when antibody-dependent enhancement (ADE)

causes a secondary infection with another serotype (4,5) Thus, a vaccine must produce balanced protection across all serotypes to be effective.

Approved Dengue Vaccines

Dengvaxia (CYD-TDV): The first approved dengue vaccine was called Dengvaxia, which was created by Sanofi Pasteur. It is a tetravalent vaccine that has been live-attenuated. A pooled effectiveness of roughly 60% was reported in clinical trials. However, studies conducted after licensure showed that seronegative recipients, especially those under nine, had a higher chance of developing severe dengue (6,7). As a result, seropositive people between the ages of 9 and 45 were only allowed limited use.

Qdenga (TAK-003): Takeda created the live-attenuated tetravalent vaccination Qdenga, which has a DENV-2 backbone. Although it was less effective against DENV-3, it protected both seropositive and seronegative persons and showed an overall efficacy of 80.2% at 12 months (8). The EU, several Latin American nations, and certain Asian nations have all authorized the vaccine (9).

Current and Emerging Clinical Trials

Butantan-DV: This live-attenuated tetravalent vaccine, created by Brazil's Instituto Butantan, is presently undergoing Phase III trials. The preliminary results have shown good immunogenicity and safety (10).

NIH TV003/TV005: The National Institutes of Health in the United States created these single-dose live attenuated vaccines, which are authorized for use in clinical studies around the world. Strong immunogenicity and seroconversion rates have been demonstrated in trials conducted in Bangladesh, Thailand, and Brazil (11).

Emerging Technologies: Research is now exploring mRNA dengue vaccines, which have the potential to offer quicker development cycles, improved safety, and customized immune responses, considering the success of mRNA platforms during the COVID-19 pandemic (12,13). Subunit, viral vectored, and DNA-based vaccines are other potential candidates in the early stages of development.

Safety and Effectiveness in Target Populations: According to systematic reviews, vaccines like CYD-TDV and TAK-003 show good safety profiles and long-lasting antibody responses, particularly in teenagers who have already been exposed to dengue. Most trial-reported adverse events were mild to severe (14,15).

Current Dengue Vaccine Trials in India

Panacea Biotec's DengiAll

10,335 people are enrolled in Phase 3 studies of Panacea Biotec's DengiAll tetravalent vaccination at 19 different sites. Effectiveness against all four dengue serotypes in India's endemic areas is assessed in this ICMR-funded study. (16) Previous stages demonstrated strong immunogenicity and safety, with seroconversion rates of 94.7%.(17)

Serum Institute's Dengusiil

Dengusiil from Serum Institute has finished Phase 1 clinical trials, demonstrating 79.5–100% seroconversion for all serotypes and 100% seroconversion for DENV-2. A good safety profile and support for additional clinical research are indicated by the absence of major adverse events. (18,19)

Challenges

Reducing antibody-dependent enhancement (ADE), especially in seronegative people, is a significant obstacle in the development of dengue vaccines.(17,20) Another issue is the durability of vaccine-induced immunity, since neutralizing antibodies may diminish with time, and booster treatments may be required.(17,21) It is crucial to ensure cost and accessibility in low-resource environments, which calls for the creation of thermostable formulations and tiered price structures.(16)

CONCLUSION

Globally, dengue still places a significant strain on public health systems, especially in tropical and subtropical areas. Even though there have been notable developments in vaccine development, such as the approval of Dengvaxia and Qdenga, issues like serotype-specific immunity, safety in seronegative populations, and long-term efficacy still exist.

For dengue-endemic nations like India, the ongoing DengiAll and Dengusiil vaccine trials in India mark a major advancement in the country's efforts to prevent dengue on its own. The future of dengue vaccinations is promising because of emerging platforms like viral vectors and mRNA. Addressing the outstanding issues with ADE, durability, and vaccination accessibility will require ongoing cooperation between ICMR, industry, and international partners. In addition to helping India, the success of these initiatives will influence dengue eradication plans around the world.

Declaration Of Generative AI And AI Assisted Technologies In The Writing Process

The authors haven't used any generative AI/AI assisted technologies in the writing process.

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